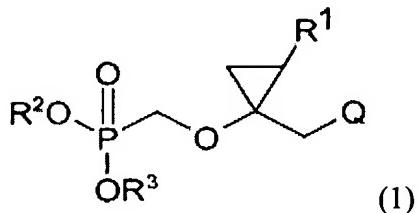


AMENDMENTS TO THE CLAIMS

1. (Original) (+)-Trans-isomers of (1-phosphonomethoxy-2-alkylcyclopropyl)methyl nucleoside derivatives represented by the following formula (1):



wherein,

R^1 represents C_1 - C_7 alkyl,

R^2 and R^3 independently of one another represent hydrogen, or represent C_1 - C_4 -alkyl

optionally substituted by one or more substituents selected from a group consisting of halogen,

C_1 - C_4 -alkoxy, phenoxy, C_7 - C_{10} -phenylalkoxy, and C_2 - C_5 -acyloxy, or represent C_2 - C_7 -acyl, C_6 -

C_{12} -aryl, C_1 - C_7 -alkylaminocarbonyl, di(C_1 - C_7 -alkyl)aminocarbonyl or C_3 - C_6 -

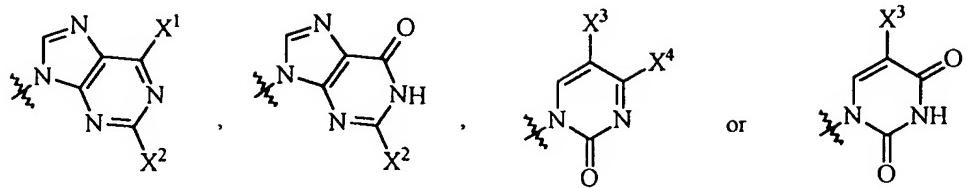
cycloalkylaminocarbonyl, or represent $-(CH_2)_m-OC(=O)-R^4$ wherein m denotes an integer of 1 to

12 and R^4 represents C_1 - C_{12} -alkyl, C_2 - C_7 -alkenyl, C_1 - C_5 -alkoxy, C_1 - C_7 -alkylamino, di(C_1 - C_7 -

alkyl)amino, C_3 - C_6 -cycloalkyl, or 3- to 6-membered heterocycle having 1 or 2 hetero atoms

selected from a group consisting of nitrogen and oxygen,

Q represents a group having the following formulae:



wherein,

X^1 , X^2 , X^3 and X^4 independently of one another represent hydrogen, amino, hydroxy, or halogen, or represent C_1 - C_7 -alkyl, C_1 - C_5 -alkoxy, allyl, hydroxy- C_1 - C_7 -alkyl, phenyl, or phenoxy, each of which is optionally substituted by nitro or C_1 - C_5 -alkoxy, or represent C_6 - C_{10} -arylthio which is optionally substituted by nitro, amino, C_1 - C_6 -alkyl, or C_1 - C_4 -alkoxy, or represent C_6 - C_{12} -arylamino, C_1 - C_7 -alkylamino, di(C_1 - C_7 -alkyl)amino, C_3 - C_6 -cycloalkylamino, or a structure of

wherein n denotes an integer of 1 or 2 and Y^1 represents O, CH_2 , or N-R (R represents C_1 - C_7 -alkyl or C_6 - C_{12} -aryl), pharmaceutically acceptable salts, hydrates or solvates thereof.

2. (Original) The compounds of claim 1 wherein the pharmaceutically acceptable salt is salt with sulfuric acid, methanesulfonic acid or hydrohalic acid.

3. (Original) The compounds of claim 1 wherein

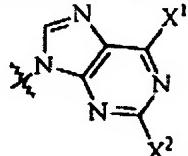
R¹ represents C₁-C₃ alkyl,

R² and R³ independently of one another represent hydrogen, or represent C₁-C₄-alkyl optionally

substituted by one or more substituents selected from a group consisting of fluorine, C₁-C₄-

alkoxy, and phenoxy, or represent -(CH₂)_m-OC(=O)-R⁴ wherein m denotes an integer of 1 to 12,

and R⁴ represents C₁-C₅-alkyl or C₁-C₅-alkoxy,



Q represents wherein, X¹ represents hydrogen, hydroxy, amino or 4-

methoxyphenylthio, or 4-nitrophenylthio, and X² represents hydrogen or amino.

4. (Original) The compounds of claim 1 which are selected from the group consisting of the

compounds described in the following Tables 1a and 1b:

Table 1a

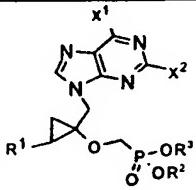
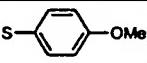
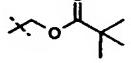
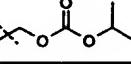
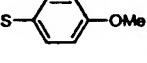
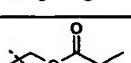
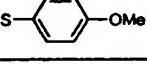
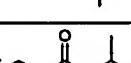
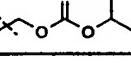
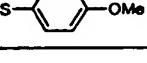
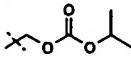
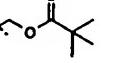
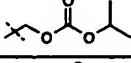
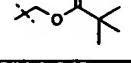
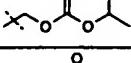
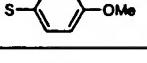
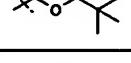
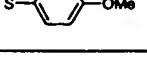
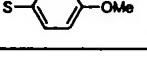
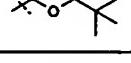
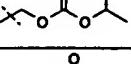
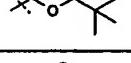
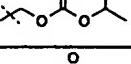
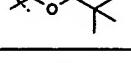
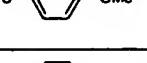
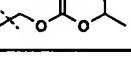
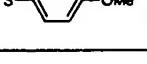
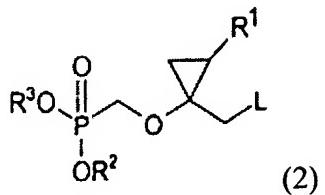
 <p>(+)-trans-optical isomer(enantiomer)</p>				
COM. NO.	R ¹	R ² & R ³	X ¹	X ²
1	CH ₃	H	OH	NH ₂
2	CH ₃	H	H	NH ₂
3	CH ₃	H	NH ₂	H
4	CH ₃	H	s- 	NH ₂
5	CH ₃	H	Cl	NH ₂
6	CH ₃		H	NH ₂
7	CH ₃		H	NH ₂
8	CH ₃		s- 	NH ₂
9	CH ₃		s- 	NH ₂
10	CH ₃		NH ₂	H
11	CH ₃		NH ₂	H
12	C ₂ H ₅	H	OH	NH ₂
13	C ₂ H ₅	H	H	NH ₂
14	C ₂ H ₅	H	NH ₂	H
15	C ₂ H ₅	H	s- 	NH ₂

Table 1b

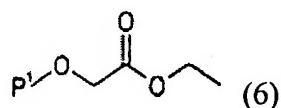
16	C ₂ H ₅	H	Cl	NH ₂
17	C ₂ H ₅		H	NH ₂
18	C ₂ H ₅		H	NH ₂
19	C ₂ H ₅		NH ₂	H
20	C ₂ H ₅		NH ₂	H
21	C ₂ H ₅			NH ₂
22	C ₂ H ₅			NH ₂
23	C ₃ H ₇	H	OH	NH ₂
24	C ₃ H ₇	H	H	NH ₂
25	C ₃ H ₇	H	Cl	NH ₂
26	C ₃ H ₇	H	NH ₂	H
27	C ₃ H ₇	H		NH ₂
28	C ₃ H ₇		H	NH ₂
29	C ₃ H ₇		H	NH ₂
30	C ₃ H ₇		NH ₂	H
31	C ₃ H ₇		NH ₂	H
32	C ₃ H ₇			H
33	C ₃ H ₇			H
34	CH ₃	iso-propyl	Cl	NH ₂
35	C ₂ H ₅	iso-propyl	Cl	NH ₂

5. (Currently Amended) A process for preparing a compound represented by the following formula (2):

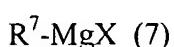


in which R¹, R² and R³ are defined as in claim 1, and L represents methanesulfonyloxy, p-toluenesulfonyloxy, or halogen, characterized in that

(a) an ethylglycolate, the alcohol group of which is protected, as represented by the following formula (6):

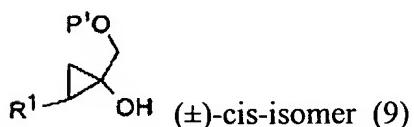
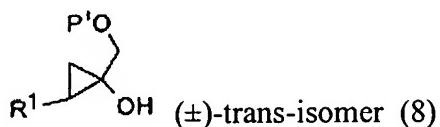


in which P¹ represents an alcohol-protecting group selected from a group consisting of benzyl(Bn), tetrahydropiranyl(THP), t-butyldiphenylsilyl(TBDPS) and t-butyldimethylsilyl(TBDMS), is reacted with alkyl magnesium halide represented by the following formula (7):



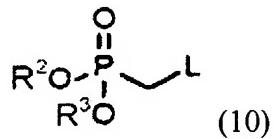
in which R^7 represents C₃-C₇ alkyl and X represents halogen, in the presence of titanium tetraisopropoxide[Ti(O*i*Pr)₄],

- (b) the resulting two cyclopropanol diastereoisomers represented by the following formulae (8) and (9):

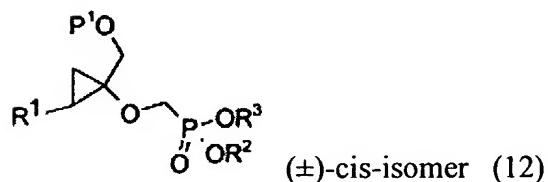
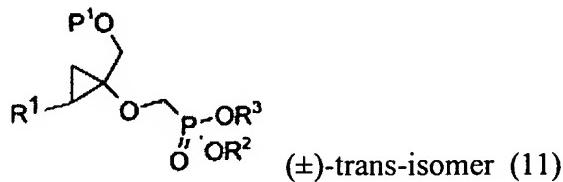


in which R¹ is defined as in claim 1 and P¹ is defined as previously described, are resolved with a silica gel column,

- (c) each compound resolved in the step (b) is subjected to an ether-forming reaction with a compound represented by the following formula (10):

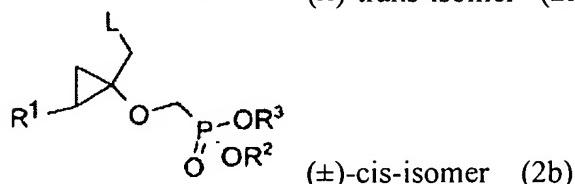
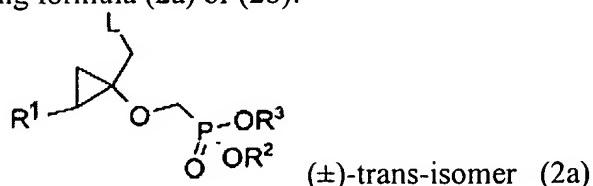


in which R² and R³ are defined as in claim 1, and L is defined as ~~in claim 5~~ previously described, in the presence of base to produce a phosphonate compound represented by the following formula (11) or (12):



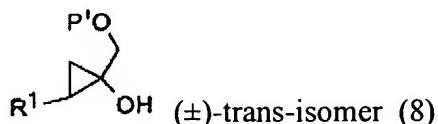
in which R¹, R² and R³ are defined as in claim 1, and P¹ is defined as previously described, and

(d) an alcohol-protecting group of the resulting compound of formula (11) or (12) is removed and a leaving group (L) is introduced to produce a compound represented by the following formula (2a) or (2b):



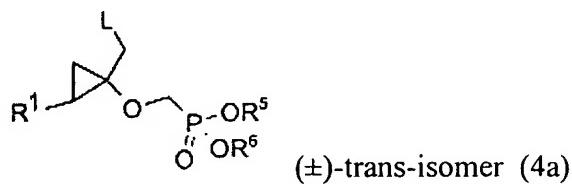
in which R¹, R² and R³ are defined as in claim 1, and L is defined as previously described.

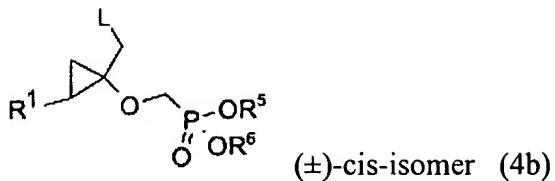
6. (Currently Amended) A compound represented by the following formula (8):



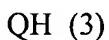
in which R¹ is defined as in claim 1, and P¹ is defined as in claim 5 represents an alcohol-protecting group selected from a group consisting of benzyl(Bn), tetrahydropiranyl(THP), t-butylidiphenylsilyl(TBDPS) and t-butyldimethylsilyl(TBDMS), and stereoisomers thereof.

7. (Currently Amended) A process for preparing stereoisomer of the compound of formula (1) as defined in claim 1 characterized in that a compound represented by the following formula (4a) or (4b):

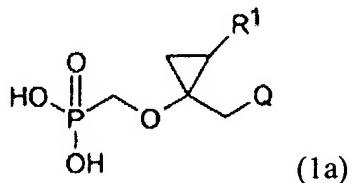




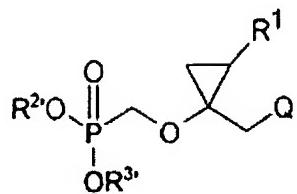
in which R¹ is defined as in claim 1, L is ~~defined as in claim 5~~ represents methanesulfonyloxy, p-toluenesulfonyloxy, or halogen, and R⁵ and R⁶ independently of one another represent C₁-C₇-alkyl, is reacted with a compound represented by the following formula (3):



in which Q is defined as in claim 1, and each compound thus obtained is resolved with a chiral column or chiral reagents to produce (+), (-) two optical isomers, each of which is present as an enantiomer enriched isomer, and then each of them is treated with trimethylsilyl bromide(TMSBr) to produce the corresponding (+), (-) two optical isomers of a compound represented by the following formula (1a):

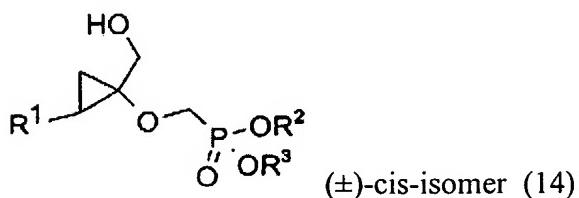
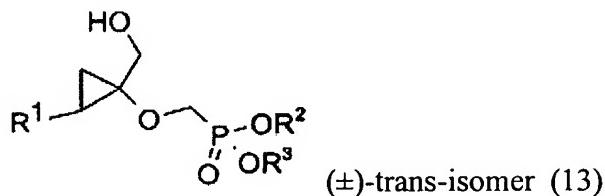


in which R¹ and Q are defined as in claim 1, and if necessary, groups R² and R³ are introduced into the compound thus obtained to produce the corresponding optical isomers of a compound represented by the following formula (1b):

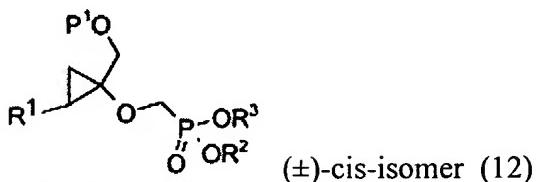
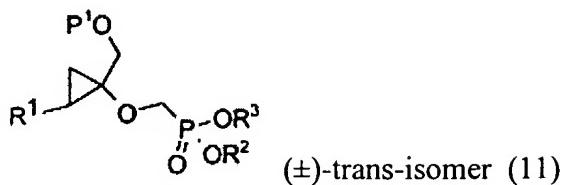


in which R^1 and Q are defined as in claim 1, and $R^{2'}$ and $R^{3'}$ represent R^2 and R^3 with the exception of hydrogen, respectively.

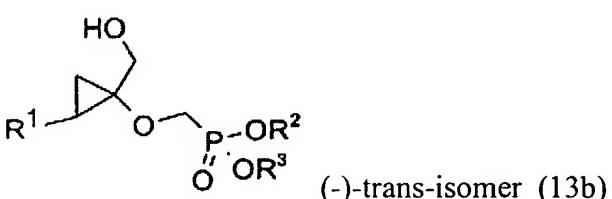
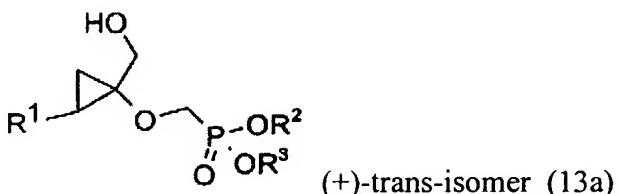
8. (Currently Amended) A process for preparing stereoisomer of the compound of formula (1) as defined in claim 1 characterized in that a compound represented by the following formula (13) or (14):

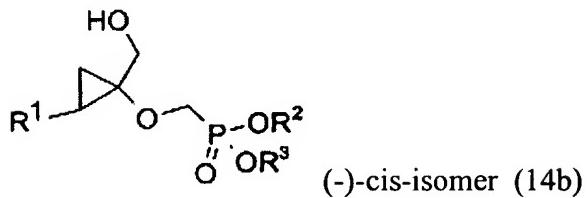
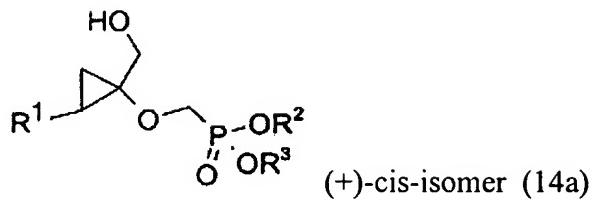


in which R^1 , R^2 and R^3 are defined as in claim 1, that is obtained by removing an alcohol-protecting group in a compound represented by the following formula (11) or (12):

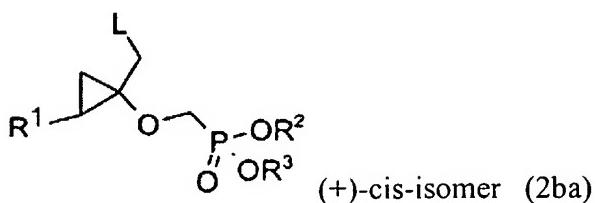
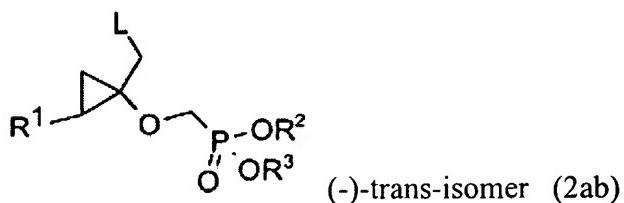
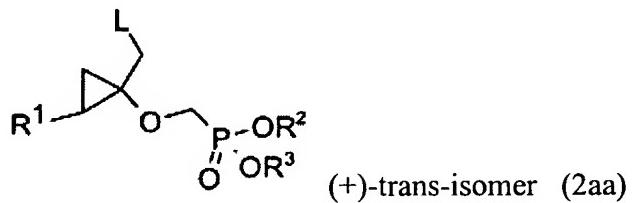


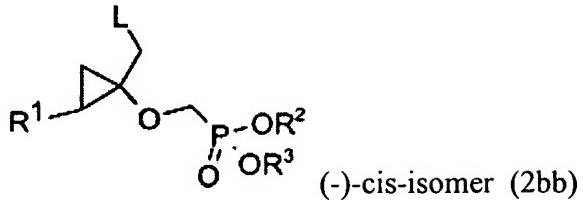
in which R¹, R² and R³ are defined as in claim 1, and P¹ is defined as in claim 5 represents an alcohol-protecting group selected from a group consisting of benzyl(Bn), tetrahydropiranyl(THP), t-butyldiphenylsilyl(TBDPS) and t-butyldimethylsilyl(TBDMS), is resolved with a hydrolase (lipase) to produce enantiomer enriched compounds represented by the following formulae (13a) and (13b) or (14a) or (14b):





in which R¹, R² and R³ are defined as in claim 1, and further an alcohol group in the compound of formula (13a), (13b), (14a) or (14b) thus obtained is replaced with a leaving group (L) to produce a compound represented by the formula (2aa), (2ab), (2ba) or (2bb):





in which R^1 , R^2 and R^3 are defined as in claim 1, and L is defined as in claim 5

represents methanesulfonyloxy, p-toluenesulfonyloxy, or halogen, and the resulting compound is reacted with a compound represented by the formula (3):

QH (3)

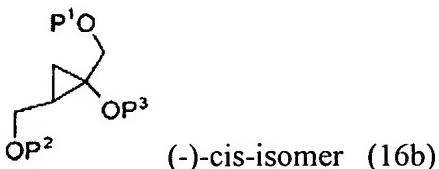
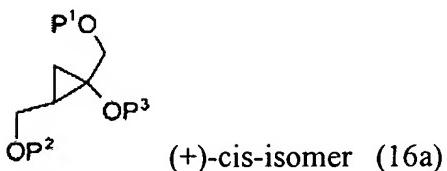
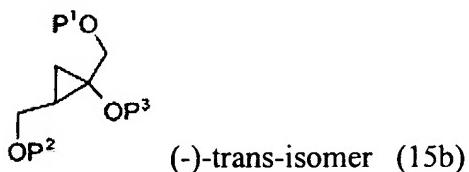
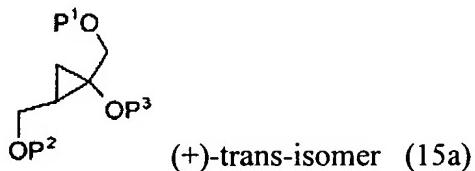
in which Q is defined as in claim 1, to produce the enantiomer enriched compound of formula (1).

9. (Currently Amended) A process for preparing stereoisomer of the compound of formula (1) as defined in claim 1 characterized in that

- aa) an alcohol-protecting group (P^2) is introduced into (+)-(methylenecyclopropyl)carbinol or (-)-(methylenecyclopropyl)carbinol, whose absolute configuration is known,

- bb) the resulting compound is subjected to dihydroxylation reaction,

cc) an alcohol-protecting group (P^1) is introduced into the primary hydroxy group in the compound obtained in the above bb) step and an alcohol-protecting group (P^3) is introduced into the tertiary hydroxy group to produce a compound represented by the formula (15a), (15b), (16a) or (16b):

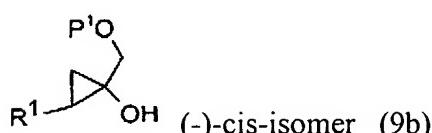
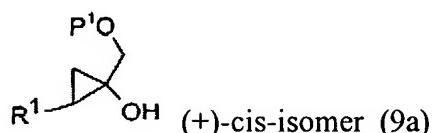
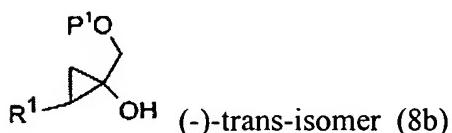
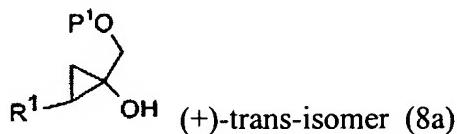


in which P^1 is defined as in claim 7 represents an alcohol-protecting group selected from a group consisting of benzyl(Bn), tetrahydropiranyl(THP), t-butyldiphenylsilyl(TBDPS) and t-butyldimethylsilyl(TBDMS), P^2 represents benzyl, benzoyl, 4-methoxybenzyl, methyloxybenzyl,

methyloxymethyl or trityl and P³ represents 1-methoxyacetyl, acetyl or 2-(trimethylsilyl)-1-ethanesulfony,

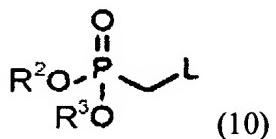
dd) the protecting group (P²) in the resulting compound is removed selectively, the leaving group (L) is introduced, and the compound thus obtained is subjected to a reduction reaction or substituted with C₁-C₇-alkyl group,

ee) the protecting group (P³) in the compound thus obtained in the above dd) step is removed to produce a compound represented by the following formula (8a), (8b), (9a) or (9b):

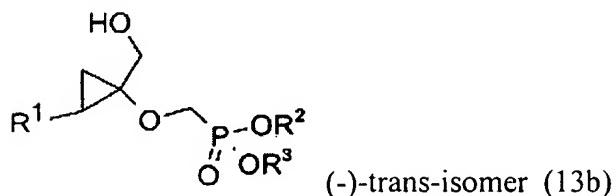
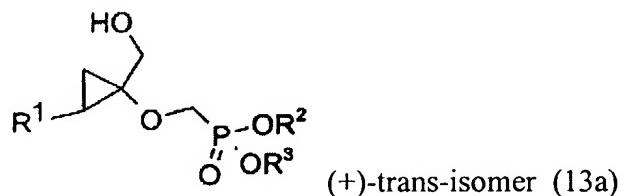


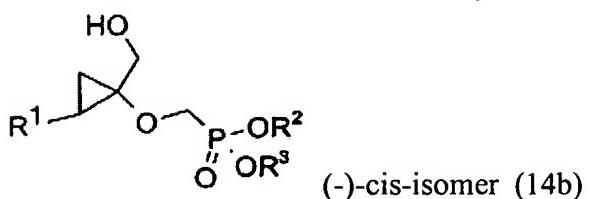
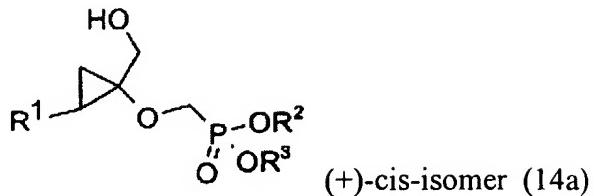
in which R¹ is defined as in claim 1, and P¹ is ~~defined as in claim 5~~ represents an alcohol-protecting group selected from a group consisting of benzyl(Bn), tetrahydropiranyl(THP), t-butylidiphenylsilyl(TBDPS) and t-butyldimethylsilyl(TBDMS),

ff) the resulting compound in the above step ee) is reacted with a phosphonate compound represented by the following formula (10):



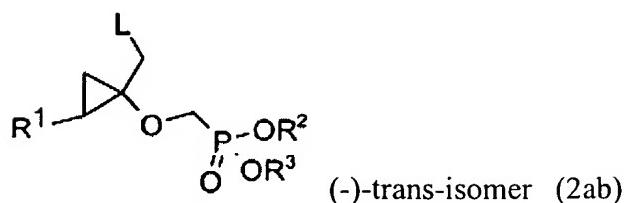
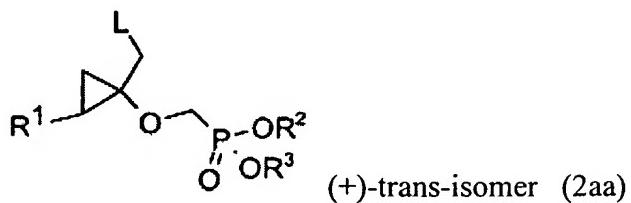
in which R² and R³ are defined as in claim 1, and L is ~~defined as in claim 5~~ represents methanesulfonyloxy, p-toluenesulfonyloxy, or halogen, and the protecting group (P¹) of the compound thus obtained is removed to produce a compound represented by the following formula (13a), (13b), (14a) or (14b):

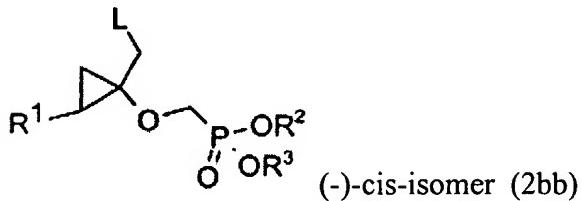
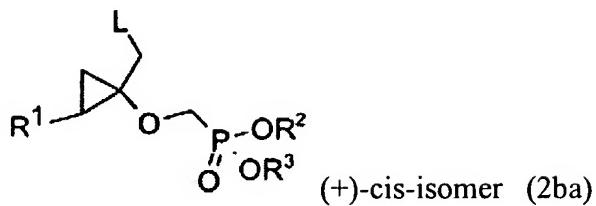




in which R¹, R² and R³ are defined as in claim 1,

gg) an alcohol group of the resulting compound is replaced with the leaving group (L) to produce a compound represented by the following formula (2aa), (2ab), (2ba) or (2bb):





in which R^1 , R^2 and R^3 are defined as in claim 1, and L is ~~defined as in claim 5~~

represents methanesulfonyloxy, p-toluenesulfonyloxy, or halogen, and

hh) the resulting compound is reacted with a compound represented by the following formula (3):

QH (3)

in which Q is defined as in claim 1, to produce the enantiomer enriched compound of formula (1).

10. (Original) A composition for the treatment of viral diseases, which comprises as an active ingredient (+)-trans-isomer of (1-phosphonomethoxy-2-alkylcyclopropyl)methyl nucleoside derivative of formula (1) as defined in claim 1, pharmaceutically acceptable salt, hydrate, or solvate thereof together with the pharmaceutically acceptable carrier.

11. (Original) A composition for the treatment of hepatitis B, which comprises as an active ingredient (+)-trans-isomer of (1-phosphonomethoxy-2-alkylcyclopropyl)methyl nucleoside derivative of formula (1) as defined in claim 1, pharmaceutically acceptable salt, hydrate, or solvate thereof together with the pharmaceutically acceptable carrier.